J Anesth (2007) 21:304–310
DOI 10.1007/s00540-007-0507-0

Journal of
Anesthesia

Prognostic value of serum myoglobin in patients after cardiac surgery

Denis Hofmann, Marco Buettner, Florian Rissner, Manuela Wahl, and Samir G. Sakka

Department of Anesthesiology and Intensive Care Medicine, Friedrich-Schiller-University of Jena, Jena, Germany

Abstract
Purpose. Serum myoglobin as a marker of myocardial damage and injury has been shown to be of prognostic value in patients with cardiovascular events. In this study, we analyzed the prognostic value of serum myoglobin in comparison to other parameters of muscle damage and renal function in patients after cardiac surgery.
Methods. We retrospectively analyzed data from 373 cardiac surgical patients (mean age, 66 ± 10 years; range, 30–88 years) by using the highest levels of serum myoglobin, creatinine, and creatine phosphokinase (CK) within the first 24 h after admission to the Intensive Care Unit (ICU). Patients' severity of illness was assessed by the Acute Physiology and Chronic Health Evaluation (APACHE) II score. Predictive properties, in terms of ICU mortality and need for renal replacement therapy (RRT), were analyzed by receiver operating characteristics (ROC) statistics and described by the area under the curve (AUC).
Results. Serum myoglobin was significantly higher in nonsurvivors ($n = 29$) than in survivors ($n = 344$; median, 1449 vs 356 $\mu g \cdot l^{-1}$; $P < 0.001$). With respect to ICU mortality, AUCs were 0.81 for myoglobin, 0.80 for creatinine, and 0.63 for CK. For comparison, an AUC of 0.82 was found for the APACHE II score. In terms of the need for RRT, AUCs were 0.87 for myoglobin, 0.92 for creatinine, and 0.60 for CK. For both endpoints, the AUCs of myoglobin and creatinine were significantly higher than that for CK.
Conclusion. Serum myoglobin is associated with outcome in patients after cardiac surgery. Prediction of ICU mortality and need for RRT was comparable for myoglobin and creatinine, while both were significantly superior to CK.

Key words Myoglobin · Prognosis · Organ failure · Cardiac surgery

Address correspondence to: S.G. Sakka, Department of Anesthesiology and Intensive Care Medicine, Medical Center Cologne-Merheim, Ostmerheimerstrasse 200, D-51109, Cologne, Germany
Received: June 6, 2006 / Accepted: January 29, 2007
This work was presented, in part, at the annual meeting of the European Society of Intensive Care Medicine, October 10–13, 2004, Berlin.

Introduction

Myoglobin, a 17 800-Dalton protein molecule consisting of 153 amino acids, is present only in heart and skeletal muscular tissue. All of its biochemical functions are not yet entirely clear; however, myoglobin is considered a participant in the muscular intracellular oxygen transfer cycle. Detectable myoglobin in the serum can be derived from either the cardiac muscle or the skeletal muscular system, or both. Physiologically, myoglobin is only detectable in low concentrations in serum or urine; the reference serum level is 70–110 $\mu g \cdot l^{-1}$ [1]. In general, myoglobin serum level has been found to increase slightly after extended muscular activity, or even more after muscular injury [2–5] or during acute myocardial infarction (AMI) [6]. Furthermore, myoglobin as a marker of myocardial damage and injury has been shown to be of prognostic value in patients with cardiovascular events, i.e., acute coronary syndrome [7], acute pulmonary embolism [8], and after thrombolytic treatment for coronary syndromes [9].

In any scenario, myoglobin and other intracellular components are thought to reach the circulation due to disruption of the cellular integrity. As a consequence, there is a wide variety of possible systemic reactions secondary to myoglobin liberation, depending on the actual extent and type of damage [3]. The range varies from limited local reactions to acute organ and multiple organ failure, of which acute renal failure is frequently seen [2].

One major clinical point of interest, e.g., during AMI, is that myoglobin reaches its peak serum level hours before other heart-muscle specific markers, such as creatine phosphokinase isoenzyme MB (CK-MB) [10–13]. Consequently, serum myoglobin has found its place in clinical routine as a determinant in diagnosing AMI [14] or acute coronary syndromes [15]. Furthermore, serum myoglobin has been suggested as a postoperative marker of graft failure in cardiac bypass operations [16]

and after thrombolytic treatment [9,14]. There are numerous studies on the value of serum myoglobin in the cardiology literature; in particular, studies which have compared serum myoglobin and CK-MB levels in the diagnosis of AMI [14,17].

In general, serum myoglobin peak levels are considered to reflect the extent of muscle damage and organ dysfunction, based on the assumption that myoglobin reaches the circulation after muscle injury in a quantity that is proportional to the tissue damage. However, there is still a lack of studies on the prognostic value of myoglobin in surgical patients in general. So far, data are available for vascular surgical patients, i.e., hypermyoglobinemia has been ascribed as a sign of successful arterial embolectomy [18]. The myoglobin serum level as a marker of organ failure has been described in a retrospective study in 29 vascular surgical patients [5]. The purpose of our study was to determine and compare the prognostic value of serum myoglobin with other parameters, in terms of ICU mortality and need for renal replacement therapy (RRT) in patients after cardiac surgery.

Patients and methods

With the approval of our ethics committee, we retrospectively analyzed the data of 373 patients (120 female, 253 male; mean age, 66 ± 10 years, range, 30–88 years) who were admitted to our intensive care unit (ICU) for postoperative care after cardiac surgery between April 1998 and May 2002. Patients underwent the following surgical procedures: valve replacement or repair (n = 84), coronary artery bypass grafting (n = 225), or a combination of both (n = 25). Eleven patients underwent heart transplantation and 28 patients had other interventions, i.e. pericardectomy, atrial thrombectomy, or closure of intracardiac septum defects. In this analysis, we included patients in whom, due to clinical indications serum myoglobin was measured. All these patients were admitted to the ICU for postoperative care as already planned prior to surgery. Intraoperative complications with a probably longer ICU length of stay or specific treatment different from the usual were not a prerequisite for enrolment in the study. The primary endpoint of our study was outcome, which was defined as ICU mortality. The need for RRT was considered as a secondary study endpoint. For clarification, the decision for RRT was not dependent on serum myoglobin levels, and serum myoglobin levels were not blinded in our study. Renal replacement therapy was initiated clinically due to otherwise uncontrollable hyperkalemia or oliguria (urinary output <500 ml per day).

On average, serum myoglobin was determined twice (mean, 1.63; range, 1–5 times; median, 2) within the first 24 h. For statistical analysis, the highest serum values for myoglobin, creatinine, and CK within the first 24 h after ICU admission were used. In our Department of Clinical Chemistry, serum myoglobin was determined by immunoassay (Beckman Coulter, Krefeld, Germany). However, there is still no standardized myoglobin reference level or a commonly used method of indexing with respect to individual measures. Because muscle weight may differ between males and females, most muscle-originated components, such as CK, do have a gender-specific normal range [19]. For instance, the manufacturer of our test kit proposes different ranges of myoglobin levels in healthy males (17.4–105.7 $\mu g \cdot l^{-1}$) and females (14.3–65.8 $\mu g \cdot l^{-1}$). In our analysis, we therefore compared serum myoglobin levels between genders. According to our laboratory, normal reference ranges are 72–127 $\mu mol \cdot l^{-1}$ for serum creatinine and less than 3.17 $\mu mol \cdot l^{-1} \cdot s^{-1}$ for serum CK, respectively. Furthermore, we included serum bilirubin and lactate as parameters of liver function and global oxygen transport. We decided not to use CK-MB for comparison with serum myoglobin, because this study was intended to analyze myoglobin as a global marker of muscle and not exclusively cardiac damage. The individual severity of illness was assessed by using the Acute Physiology and Chronic Health Evaluation (APACHE) II score [20].

Statistical analysis

If not stated otherwise, all results are given as means ± SD (median). Statistical comparisons between survivors and nonsurvivors, as well as those between males and females, were performed by using a nonparametric (Mann-Whitney U) test. Receiver-operating characteristics (ROC) curves were constructed for myoglobin, creatinine, CK, and the APACHE II score to analyze and compare the area under the curve (AUC), which is a measure for the predictive power of each marker. The sensitivity and specificity of each parameter with respect to survival and the need for RRT were analyzed by ROC statistics. AUCs for the different parameters were compared against each other. The plot of the ROC statistic shows the true-positive rate against the false-positive rate for the different possible cutoff points of a diagnostic test. The AUC is a measure of test accuracy. For each parameter, the cutoff value was calculated, representing the highest accuracy (minimal false-negative and false-positive results). A three-dimensional (3D) box-and whiskers plot was constructed for serum myoglobin with respect to ICU mortality and need for RRT. For data storage, descriptive and explorative statistics, and calculation of ROC curves, SPSS for Windows version 12.0 (SPSS, Chicago, IL, USA) was used. Comparison between AUCs of the

different parameters was performed with MedCalc for Windows version 8.1.1 (Mariakerke, Belgium). A value of $P < 0.05$ was considered statistically significant.

Results

Overall results are summarized in Table 1. In males, myoglobin was between 32 and 175 090 (1869 ± 11 373; median, 387) $\mu g \cdot l^{-1}$. In females, myoglobin was between 15 and 40 809 (1714 ± 5642; median 395) $\mu g \cdot l^{-1}$. There was no statistically significant difference between the two subgroups ($P = 0.82$). On average, myoglobin peak level was recorded 12 ± 7.5 (range, 0–23.9, median, 14.4) h after ICU admission. Notably, the patient who developed a serum myoglobin of 175 090 $\mu g \cdot l^{-1}$ was male. Without this extreme outlier, who died, myoglobin levels in males were between 32 and 24 275 (387) $\mu g \cdot l^{-1}$. As a measure of duration of surgery, we analyzed duration of extracorporeal circulation (mean, 115 ± 50 min), aortic cross-clamping time (64 ± 29 min), and reperfusion (41 ± 24 min). There was no correlation between serum myoglobin level and duration of extracorporeal circulation ($r = 0.15$), aortic cross-clamping time ($r = 0.05$); or duration of reperfusion ($r = 0.27$) Similar findings also applied to CK and extracorporeal circulation times ($r = 0.15$, $r = 0.00$, and $r = 0.24$). It was noteworthy that linear regression analysis revealed no correlation between myoglobin and CK-MB levels ($r = 0.37$), while a correlation between myoglobin and CK was found ($r = 0.70$, $P < 0.001$).

The analysis between survivors and nonsurvivors revealed significant differences for age ($P = 0.03$), APACHE II score ($P < 0.001$), length of ICU stay ($P = 0.02$), and need for RRT ($P < 0.001$). Furthermore, serum creatinine, CK, bilirubin, lactate, and myoglobin were significantly different between these two subpopulations (Table 2).

With respect to prediction of ICU mortality, ROC statistics revealed AUCs of 0.81 for myoglobin, 0.80 for creatinine, and 0.63 for CK (Fig. 1). For comparison, the AUC for the APACHE II score as a complex instrument of ICU outcome prediction was 0.82. With respect to ICU mortality, the cutoff value (highest sensitivity and specificity) for myoglobin was 537.0 $\mu g \cdot l^{-1}$. Without the outlier mentioned above, ROC statistics revealed AUCs of 0.80 for creatinine, 0.62 for CK, 0.80 for myoglobin, and 0.81 for the APACHE II score. Comparison of the different AUCs revealed no significant difference between myoglobin and creatinine ($P = 0.96$), while

Table 1. Patients' demographics and overall results

	Results
n	373 (120 female, 253 male)
Age [years]	66 ± 10 (30–88)
APACHE II score	20 ± 7 (6–50)
Length of ICU stay [days]	5.6 ± 9.1 (1–62)
Renal replacement therapy, *n*	41 [11%]
Nonsurvivors, *n*	29 [8%]
Myoglobin [$\mu g \cdot l^{-1}$]	1819 ± 9890 (15–175 090)
Creatinine [$\mu mol \cdot l^{-1}$]	148 ± 114 (57–937)
Creatine phosphokinase [$\mu mol \cdot l^{-1} \cdot s^{-1}$]	7.7 ± 18.2 (0.16–240)
Bilirubin [$\mu mol \cdot l^{-1}$]	18.9 ± 9.8 (5.5–72.4)
Lactate [$mmol \cdot l^{-1}$]	4.5 ± 3.9 (0.7–37.0)

Values are means ± SD (ranges)

Table 2. Patients' demographics, and results in survivors and nonsurvivors, as defined by ICU mortality

	Survivors	Nonsurvivors
n	344	29
Age [years]	66 ± 10 (67; 30–88)	70 ± 10 (71; 46–85)**
APACHE II score	20 ± 7 (19; 6–38)	29 ± 8 (28; 14–50)*
Length of ICU stay [days]	5.0 ± 7.8 (3; 1–57)	12.4 ± 17.4 (5; 1–62)**
Renal replacement therapy, *n*	21 [7%]	20 [69%]*
Myoglobin [$\mu g \cdot l^{-1}$]	916 ± 2 520 (356; 15–29 761)	12 530 ± 33 058 (1449; 147–175 090)*
Creatinine [$\mu mol \cdot l^{-1}$]	142 ± 114 (111; 57–937)	217 ± 102 (188; 91–477)*
Creatine phosphokinase [$\mu mol \cdot l^{-1} \cdot s^{-1}$]	6.7 ± 13.6 (3.6; 0.16–218)	19.3 ± 44.5 (4.7; 0.37–240)**
Bilirubin [$\mu mol \cdot l^{-1}$]	18.0 ± 9.1 (15.6; 5.5–72.4)	28.8 ± 12.0 (28.5; 11.6–60.2)*
Lactate [$mmol \cdot l^{-1}$]	4.1 ± 3.2 (2.8; 0.7–22.0)	9.6 ± 6.7 (7.8; 1.9–37.0)*

* Mann-Whitney *U*-test ($P < 0.001$); ** Mann-Whitney *U*-test ($P < 0.05$)
Values are means ± SD (median; range)

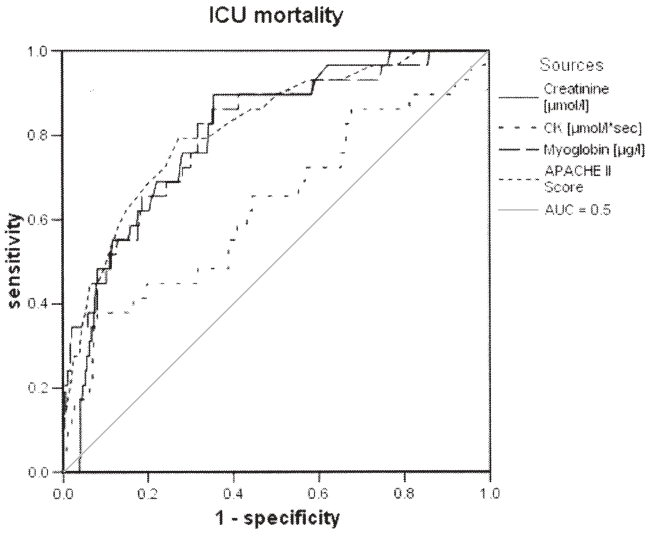

Fig. 1. Receiver operating characteristics (ROC) statistics, with respect to intensive care unit (*ICU*) mortality, for serum myoglobin, creatinine, creatine phosphokinase (*CK*), and the Acute Physiology and Chronic Health Evaluation (*APACHE*) II score. *AUC*, area under the curve

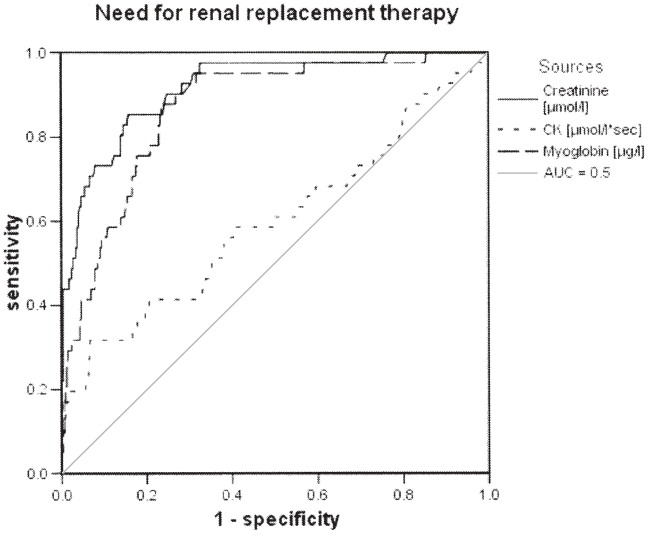

Fig. 2. Receiver operating characteristics (ROC) statistics, with respect to renal replacement therapy, for serum myoglobin, creatinine, and creatine phosphokinase (*CK*). *AUC*, area under the curve

both myoglobin ($P < 0.001$) and creatinine ($P = 0.004$) were superior to CK. For comparison, the APACHE II score was superior to CK ($P = 0.004$), but not to myoglobin ($P = 0.82$) and creatinine ($P = 0.79$).

With regard to RRT, ROC statistics revealed AUCs of 0.87 for myoglobin, 0.92 for creatinine, and 0.60 for CK (Fig. 2). A cutoff value of 544 µg·l^{-1} was calculated for myoglobin. Multiple comparison of the AUCs revealed no significant difference between myoglobin and

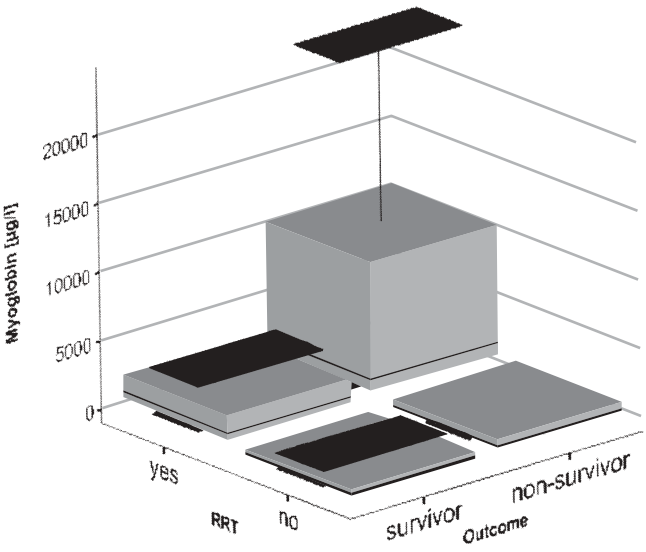

Fig. 3. Box-and-whiskers-plot created with respect to ICU mortality and renal replacement therapy (*RRT*). Displayed without outliers and extreme values. *The flat black rectangles* show medians

creatinine ($P = 0.22$), while both myoglobin ($P < 0.001$) and creatinine ($P < 0.001$) were superior to CK. Results of ROC statistics for each variable, with respect to RRT, are presented in Table 3. Furthermore, we plotted myoglobin values with respect to outcome and need for RRT. Serum myoglobin was obviously highest in nonsurvivors who required RRT, lower in survivors with RRT, and lowest in survivors without the need for RRT (Fig. 3).

Discussion

The results of our study demonstrate that serum myoglobin is of similar prognostic value to serum creatinine in cardiac surgical patients. By using the most pathological values within the first 24 h after ICU admission, creatinine and myoglobin showed significantly better predictive values for outcome than serum CK. These findings are in congruence with a very recent study in 47 critically ill patients, performed by Mikkelsen and Toft [13], who also found earlier peaking and better prognostic properties of myoglobin in comparison to CK.

In general, myoglobin, CK, and troponin are intracellular components with their origin in muscle, but they are not specific to the myocardial muscle. Different causes of muscle damage can lead to different time courses of the production and elimination of these components, e.g., administration of succinylcholine, following acute myocardial infarction (AMI), or malignant hypertension [3].

Table 3. Area under the curve (AUC) and cutoff value (sensitivity, specificity) for each variable

ROC for ICU mortality		Asymptotic 95% confidence interval		
Variable	AUC	Lower limit	Upper limit	Cutoff value (sensitivity, specificity [%])
Myoglobin [$\mu g \cdot l^{-1}$]	0.81	0.72	0.89	537 (82.8, 68.3)
Creatinine [$\mu mol \cdot l^{-1}$]	0.80	0.73	0.88	124 (64.5, 89.7)
CK [$\mu mol \cdot l^{-1} \cdot s^{-1}$]	0.63	0.51	0.75	13.7 (91.9, 37.9)
APACHE II score	0.82	0.74	0.90	23 (72.2, 79.3)
ROC for RRT		Asymptotic 95% confidence interval		
Variable	AUC	Lower limit	Upper limit	Cutoff value (sensitivity, specificity [%])
Myoglobin [$\mu g \cdot l^{-1}$]	0.87	0.72	0.92	544 (92.7, 71.1)
Creatinine [$\mu mol \cdot l^{-1}$]	0.92	0.87	0.96	152 (85.4, 84.3)
CK [$\mu mol \cdot l^{-1} \cdot s^{-1}$]	0.60	0.49	0.70	14.2 (31.7, 93.4)

RRT, renal replacement therapy; CK, creatine phosphokinase; APACHE, Acute Physiology and Chronic Health Evaluation

So far, CK-MB has been described to be superior to myoglobin with respect to diagnostic value [15]. In the study of Collinsons et al. [15], most patients had AMI, or unstable or stable angina, and only 30 patients were admitted with multiple trauma: in those patients, myoglobin (mean, about 100 $\mu g \cdot l^{-1}$) increased more than CK-MB and cardiac troponin T (cTnT) [15]. However, major reasons for this difference, in contradiction to the findings of our study, were that the mass of an isoenzyme of CK (i.e., CK-MB) and not serum CK was measured in that study [15]. Moreover, CK-MB mass was used as a diagnostic tool for the verification of AMI, but not for outcome prediction. Per se, CK-MB mass is considered to be more or less specific for cardiac events. In the study of Collinson et al. [15], values were obtained at defined time points within the initial 24 h after admission. In contrast, we measured CK instead of CK-MB, and used the most pathological value for each parameter during this time period. We see this decision confirmed by the missing correlation between myoglobin and CK-MB peak levels. Our patients, however, were not medical but cardiac surgical patients, which means their acute phase and, thus, peak serum levels of the analyzed parameters may not have been detected appropriately. Therefore, the peak levels in our study resulted mainly from surgical interventions which were presumed to cause less damage than an infarction, acute trauma, or a different surgical intervention would do in the same area. In our study, we had a relatively wide range of myoglobin peak time (on average, 12.0; highest, 23.9 h) that was longer than the plasma-peak time of 4–7 h as reported [14]. This finding may be interpreted as the cardiac event or cardiac surgery per se not being the only or main cause of the rising myoglobin level. This interpretation may be considered to be supported by the fact that we found no correlation between the duration of extracorporeal circulation and myoglobin levels or between these parameters and CK or CK-MB. Thus, in our setting, we did not distinguish between CK or its isoforms and the respective diagnostic or even prognostic meaning. Furthermore, we did not analyze serum myoglobin as a tool for the assessment of myocardial ischemia or patency of coronary bypass grafts. Instead, we used serum myoglobin as a global marker of muscle damage.

For the interpretation of our data, a general issue which should be considered is the elimination kinetics of myoglobin from the blood. The relatively short period of time between muscle injury and the consecutive peak serum concentration may be the most convincing benefit of myoglobin as an early marker. As already mentioned, this fact may be disadvantageous, in so far as the serum myoglobin concentration also decreases quite rapidly. Lappalainen et al. [21] demonstrated that the myoglobin serum level decreased to around 65% of the original value within 6 h, whereas serum CK is still at around 90% of the initial peak. Also, Laurence [3] described that, following muscle damage during minor or major surgery, serum myoglobin peaked earlier (within 24 h) and CK was highest on the second day. Thus, it is not surprising when some authors report that in early-type infarction cases, sole screening for myoglobin is positive, and in late-type infarctions, serum myoglobin has returned to normal values at the time of investigation [17]. Although Stoerk et al. [17] exclusively studied patients with an acute coronary syndrome, the above-mentioned constellation of findings also points out the general problem that is also discussed by Collinson et al. [15], i.e., an early peak value may be missed if there is a longer delay of any kind between

the incident and the drawing of blood samples. Collinson et al. [15] agree that myoglobin "is probably useful in an emergency department for early exclusion of myocardial infarction, but is less useful in patients admitted to hospital, as blood samples tend to be taken later". With respect to our study population, this may also apply to the duration of surgery, or a longer postoperative period due to a delayed intervention for hemodynamic instability. Unfortunately, as explained by our retrospective study design using only data obtained in the ICU, we cannot definitively address this issue.

Also, in nonsurgical patients, Lovis et al. [22] described that patients admitted to an ICU for acute severe bronchial asthma may present with an elevation of plasma CK, CK-MB, and myoglobin not related to any heart injury. This underlines another fact one has to consider when interpreting the results of serum myoglobin. Myoglobin levels may change due to many different events or eventualities.

Still, there is a lack of literature on the value of serum myoglobin in critically ill surgical patients. Fricke et al. [5] retrospectively analyzed data of 29 patients who had been treated because of extremity ischemia- reperfusion damage. Their retrospective analysis showed that the myoglobin serum level permitted a prognosis about the extent of the expected impairment after revascularization. These authors divided the patients into two groups: one group, with myoglobin less than 20000 $\mu g \cdot l^{-1}$ showed a mortality of about 11%, whereas the other group, with myoglobin more than 20000 $\mu g \cdot l^{-1}$ had a mortality of about 64%. Moreover, they found an increasing number of failing organ systems. In most of the patients considered, they documented acute renal failure and disorders in cerebral nervous system functions, followed by failure of lung, liver, and the cardiovascular system. Fricke et al. [5] described a limit of 20000 $\mu g \cdot l^{-1}$ myoglobin as the critical threshold for the occurrence of apparent organ failure. Between 8 and 12 h after reperfusion, the maximum myoglobin was reached, and very high values of myoglobin (>20000 $\mu g \cdot l^{-1}$) indicated a poor prognosis, even if the patient was still in a good clinical condition. According to these authors, the high number of deaths in the patient group with a very high myoglobin level underlines the importance of the surgeon's primary decision with regard to surgical treatment (revascularization or amputation). Furthermore, it indicates the urgency to search for causal factors, further prognostic parameters, and therapeutic strategies.

In general, therapeutic measures to avoid organ failure are considered to include alkalinization and forced diuresis [21]. However, although clinical data are available that indicate that this strategy is beneficial and probably superior, in regard to elimination to extracorporeal interventions [5,23], no controlled clinical trials have been performed. The limitations of our study are that, due the retrospective design, the subpopulations of survivors and nonsurvivors differed significantly in age and severity of illness, i.e., the nonsurvivors were significantly older and also sicker than the survivors, as indicated by the APACHE II scores. Although the APACHE II score is not an ideal prognostic tool in cardiac surgical patients [24], we used this instrument to describe the severity of illness of our patients. However, we found that the nonsurvivors had an a-priori higher probability of dying during their ICU stay. Of course, many factors did influence ICU outcome in our patients and we studied only one serum parameter. Because we had different numbers of measurements per patient, we reduced our data by using the most pathological value obtained within the first 24 h after ICU admission.

One major limitation of our study is that we only enrolled patients in whom serum myoglobin was measured, a fact that, per-se, creates a selection bias. Due to the retrospective design, we could assess all cardiac surgical patients treated during the elapsed period of time. As a consequence, we can neither provide data for those patients who were not recruited, nor compare their severity of illness, outcome, and other influencing factors with these factors in our study population. Finally, we did not study the effects of specific therapeutic interventions to decrease serum myoglobin levels, and thus we cannot comment on the effectiveness of different strategies in terms of reduction in ICU mortality.

Conclusion

In patients after cardiac surgery, serum myoglobin is correlated with outcome, as non-survivors had a significantly higher serum myoglobin than survivors. The prognostic value of myoglobin, in terms of ICU mortality and need for RRT, was comparable with that of creatinine, while both were significantly superior to CK. However, our results are based on a retrospective analysis using data as obtained within the first 24 h after ICU admission, and appropriate prospective clinical studies are needed to confirm our findings.

References

1. Mair J, Artner-Dworzak E, Lechleitner P, Morass B, Smidt J, Wagner I, Dienstl F, Puschendorf B (1992) Early diagnosis of acute myocardial infarction by a newly developed rapid immunoturbidometric assay for myoglobin. Br Heart J 68:462–468
2. Holt SG, Moore KP (2001) Pathogenesis and treatment of renal dysfunction in rhabdomyolysis. Intensive Care Med 27:803–811
3. Laurence ASS (2000) Serum myoglobin and serum creatine kinase following surgery. Br J Anaesth 84:763–766

4. Koz M, Erbas D, Bilgihan A, Aricioglu A (1992) Effects of acute swimming exercise on muscle and erythrocyte malondialdehyde, serum myoglobin, and plasma ascorbic acid concentrations. Can J Physiol Pharmacol 70:1392–1395
5. Fricke P, Weiß G, Lippert H (2002) Ischemia/ reperfusion syndrome- myoglobin: its impact and role as a prognostic parameter. A retrospective analysis of clinical data. Intensivmed 39:38–46
6. Stone MJ, Waterman MR, Harimoto D, Murray G, Willson N, Platt MR, Blomqvist G, Willerson JT (1977) Serum myoglobin level as diagnostic test in patients with acute myocardial infarction. Heart 39:375–380
7. Svensson L, Axelsson C, Nordlander R, Herlitz J (2004) Prognostic value of biochemical markers; 12-lead ECG and patient characteristics amongst patients calling for an ambulance due to a suspected acute coronary syndrome. J Intern Med 255:469–477
8. Pruszczyk P, Bochowicz A, Kostrubiec M, Torbicki A, Szulc M, Gurba H, Kuczynska K, Berent H (2003) Myoglobin stratifies short-term risk in acute major pulmonary embolism. Clin Chim Acta 338:53–56
9. Iqbal MP, Kazmi KA, Mehboobali N (2004) Myoglobin—a marker of reperfusion and a prognostic indicator in patients with acute myocardial infarction. Clin Cardiol 27:144–150
10. Roxin LE, Venge P, Friman G, Hallgren R (1979) Radioimmunoassays of human myoglobin in serum and urine. Scand J Clin Lab Invest 39:37–46
11. Roxin LE, Venge P, Wide L (1980) A fast and sensitive radioimmunoassay of human myoglobin for use in the early diagnosis of heart infarction. Clin Chim Acta 107:129–134
12. Roxin LE, Cullhed I, Groth T, Hallgren T, Venge P (1984) The value of serum myoglobin determinations in the early diagnosis of acute myocardial infarction. Acta Med Scand 215:417–425
13. Mikkelsen TS, Toft P (2005) Prognostic value, kinetics and effect of CVVHDF on serum of the myoglobin and creatine kinase in critically ill patients with rhabdomyolysis. Acta Anaesthesiol Scand 49:859–864
14. Herrmann J, Volbracht L, Haude M, Eggebrecht H, Malyar N, Mann K, Erbel R (2001) Biochemical markers of ischemic and non-ischemic myocardial damage. Med Klin 96:144–156
15. Collinson PO, Stubbs PJ, Kessler AC (2003) Multicentre evaluation of the diagnostic value of cardiac troponin T, CK-MB mass, and myoglobin for assessing patients with suspected acute coronary syndromes in routine clinical practice. Heart 89:280–286
16. Thielmann M, Massoudy P, Marggraf G, Knipp S, Schmermund A, Piotrowski J, Erbel R, Jakob H (2004) Role of troponin I, myoglobin, and creatine kinase for the detection of early graft failure following coronary artery bypass grafting. Eur J Cardiothorac Surg 26:102–109
17. Stoerk T, Gareis R, Muller R, Hammerle M, Muller-Bardorff M, Braun R, Frohlich E, Koenig W, Mockel M (2001) Diagnostik und Risikostratifizierung bei Patienten mit akutem Koronarsyndrom mittels Myoglobin, Troponin T und CK/ CK-MB. Intensivmed 38:385–393
18. Andersen PT, Moller-Petersen J, Henneberg EW, Egeblad K (1987) Hypermyoglobinemia after successful arterial embolectomy. Surgery 102:25–31
19. Schumann G, Glauke R (2003) New IFCC reference procedures for the determination of catalytic activity concentrations of five enzymes in serum: preliminary upper reference limits obtained in hospitalized patients. Clin Chim Acta 327:69–79
20. Knaus WA, Draper EA, Wagner DP, Zimmerman JE (1985) APACHE II: a severity of disease classification system. Crit Care Med 13:818–829
21. Lappalainen H, Tiula E, Uotila L, Manttari M (2002) Elimination kinetics of myoglobin and creatine kinase in rhabdomyolysis: Implications for follow-up. Crit Care Med 30:2212–2215
22. Lovis C, Mach F, Unger PF, Bouillie M, Chevrolet JC (2001) Elevation of creatine kinase in acute severe asthma is not of cardiac origin. Intensive Care Med 27:528–533
23. Wakabayashi Y, Kikuno T, Ohwada T, Kikawada R (1994) Rapid fall in blood myoglobin in massive rhabdomyolysis and acute renal failure. Intensive Care Med 20:109–112
24. Hekmat K, Kroener A, Stuetzer H, Schwinger RH, Kampe S, Bennink GB, Mehlhorn U (2005) Daily assessment of organ dysfunction and survival in intensive care unit cardiac surgical patients. Ann Thorac Surg 79:1555–1562